



Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV.

Downloaded from <https://aidsinfo.nih.gov/guidelines> on 8/31/2020

Visit the AIDSinfo website to access the most up-to-date guideline.

Register for e-mail notification of guideline updates at <https://aidsinfo.nih.gov/e-news>.

Introduction (Last updated May 29, 2018; last reviewed June 26, 2019)

Opportunistic infections (OIs) were the first clinical manifestations that alerted clinicians to the occurrence of the acquired immunodeficiency syndrome (AIDS). *Pneumocystis pneumonia* (PCP), toxoplasma encephalitis, cytomegalovirus (CMV) retinitis, cryptococcal meningitis, tuberculosis, disseminated *Mycobacterium avium* complex (MAC) disease, and pneumococcal respiratory disease, as well as certain cancers such as Kaposi sarcoma and central nervous system lymphoma, have been hallmarks of AIDS. These OIs, and many more, occurred on average 7 to 10 years after infection with HIV.^{1,2} Until effective antiretroviral therapy (ART) was developed, patients generally survived only 1 to 2 years after the initial manifestation of AIDS.³

HIV-related OIs have been defined as infections that are more frequent or more severe because of HIV-mediated immunosuppression.⁴

Starting in the late 1980s, the use of chemoprophylaxis, immunization, and better strategies for managing OIs improved quality of life and lengthened survival of persons with HIV.⁵ Early antiretroviral drugs and treatment strategies added further benefit.⁶ However, the introduction of highly effective combination ART in the mid-1990s has had the most profound influence on reducing OI-related morbidity and mortality in persons with HIV.⁷⁻¹¹

Despite the availability of multiple safe, effective, and simple ART regimens, and a corresponding steady decline in the incidence of OIs,¹¹ the Centers for Disease Control and Prevention (CDC) estimates that more than 40% of Americans with HIV are not effectively virally suppressed.¹²⁻¹⁷ As a result, OIs continue to cause preventable morbidity and mortality in the United States.¹⁸

Achieving and maintaining durable viral suppression in all people with HIV, and thus preventing or substantially reducing the incidence of HIV related OIs, remains challenging for three main reasons:

- *Not all HIV infections are diagnosed, and once diagnosed many persons have already experienced substantial immunosuppression.* CDC estimates that in 2015, 15% of the people with HIV in the United States were unaware of their infections.¹⁹ Among those with diagnosed HIV, more than 50% had had HIV for more than 3 years²⁰ and approximately 20% had a CD4 T lymphocyte (CD4) cell count <200 cells/mm³ (or <14%) at the time of diagnosis.^{20,21}
- *Not all persons with diagnosed HIV receive timely continuous HIV care or are prescribed ART.* CDC estimates that in 2015, 16% of persons with newly diagnosed HIV had not been linked to care within 3 months and among persons living with HIV only 57% were adequately engaged in continuous care.²¹
- *Not all persons treated for HIV achieve durable viral suppression.* CDC estimates that in 2014, only 49% of diagnosed patients were effectively linked to care and had durable viral suppression.²² Causes for the suboptimal response to treatment include poor adherence, unfavorable pharmacokinetics, or unexplained biologic factors.^{23,24}

Thus, some persons with HIV infection will continue to present with an OI as the sentinel event leading to a diagnosis of HIV infection or present with an OI as a complication of unsuccessful viral suppression.

Durable viral suppression eliminates most but not all OIs. Tuberculosis, pneumococcal disease, and dermatomal zoster are examples of infectious diseases that occur at higher incidence in persons with HIV regardless of CD4 count. The likelihood of each of these OIs occurring does vary inversely with the CD4 count, however.²³⁻³¹

When certain OIs occur—most notably tuberculosis and syphilis—they can increase plasma viral load,³²⁻³⁷ which both accelerates HIV progression and increases the risk of HIV transmission.

Thus, clinicians continue to need to be knowledgeable about the prevention and management of HIV-related OIs.

History of These Guidelines

In 1989, the Guidelines for Prophylaxis Against *Pneumocystis carinii* Pneumonia for Persons Infected with the Human Immunodeficiency Virus became the first HIV-related treatment guideline published by the U.S. government.³⁸ This guideline was published in the Morbidity and Mortality Weekly Report (MMWR), which was the most rapid mode of publication at the time. It was followed by a guideline on prevention of *Mycobacterium avium* complex disease in 1993.³⁹ In 1995, these guidelines were expanded to include the treatment of 18 HIV-related OIs. In 2004, information about the prevention of HIV-related OIs was incorporated into the guidelines. The NIH, the CDC, and the HIV Medicine Association (HIVMA) of the Infectious Diseases Society of America (IDSA) now jointly co-sponsor these guidelines,^{4,40-42} which have been published in peer-reviewed journals and/or the MMWR in 1997, 1999, and 2002.⁴¹⁻⁵³ Since 2009, the guidelines have been managed as a living document on the web with each chapter reviewed quarterly by the guidelines committee. Updates are published as often and as promptly as deemed appropriate by the guidelines committee.

Data regarding the use of these guidelines demonstrate that the document is a valuable reference for HIV health care providers. In 2017, there were almost 423,075 page views of the online version of the guidelines, and almost 4,000 pdf downloads.

All guideline recommendations regarding therapy and prevention are rated in terms of the quality of supporting evidence; comments about diagnosis are not rated. These ratings allow readers to assess the relative importance of each recommendation. This document focuses on adults and adolescents; recommendations for children with HIV can be found in separate documents at <https://aidsinfo.nih.gov>.

These guidelines are intended for clinicians, other health care providers, patients with HIV, and policy makers in the United States. Guidelines pertinent to other regions of the world, especially resource-limited countries, may differ with respect to the spectrum of relevant OIs and the diagnostic and therapeutic options that are available to clinicians.

Guidelines Development Process

These guidelines were prepared by the OI Working Group under the auspices of the Office of AIDS Research Advisory Council (OARAC), an authorized Federal Advisory Committee to the U.S. Department of Health and Human Services established in 1994. Briefly, co-editors who are selected and appointed by their respective agencies or organizations (i.e., NIH, CDC, IDSA) convene OI specific working groups of clinicians and scientists with subject matter expertise in those specific OIs. The co-editors appoint a leader for each working group. The working groups review in real time the relevant literature published since the last review of the guidelines and, if indicated, propose revised recommendations, which are then presented to the co-editors and other working group leaders. The co-editors and working group leaders have a teleconference quarterly to determine changes in each section that are indicated. The co-editors also convene a meeting of subject group leads at ID Week each year to review progress and set an agenda for the coming year. Final guidelines revisions posted on the *AIDSinfo* website may include additional changes made by the co-editors under the advisement of Office of AIDS Research Advisory Committee (OARAC).

The names and affiliations of all contributors as well as their financial disclosures are provided in [Panel Roster](#) and [Financial Disclosures](#) (Appendix C).

Guidelines Development Process	
Topic	Comment
Goal of the guidelines	Provide guidance to HIV care practitioners and others on the optimal prevention and management of HIV-related opportunistic infections (OIs) for adults and adolescents in the United States.
Panel members	The Panel is composed of co-editors who represent the National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC), and the HIV Medicine Association of the Infectious Disease Society of America (HIVMA/IDSA), plus Panel members with expertise in HIV clinical care, infectious disease management, and research. Co-editors are appointed by their respective agencies or organizations. Panel members are selected from government, academia, and the healthcare community by the co-editors and assigned to a working group for one or more of the guideline sections based on the member's area of subject matter expertise. Each working group is chaired by a Panel member selected by the co-chairs. Members serve on the Panel for a 3-year term, with an option to be reappointed for additional terms. Prospective Panel members may self-nominate at any time. When specific or unique subject matter expertise is required, the co-editors together with working group leaders may solicit advice from individuals with such specialized knowledge. The list of the current Panel members can be found in Appendix C .
Financial disclosure and management of conflicts of interest	All members of the Panel submit a written financial disclosure annually reporting any associations with manufacturers of drugs, vaccines, medical devices, or diagnostics used to manage HIV-related OIs. A list of these disclosures and their last update is available in Appendix C . The co-editors review each reported association for potential conflicts of interest and determine the appropriate action: disqualification from the Panel, disqualification or recusal from topic review and discussion, or no disqualification needed. A conflict of interest is defined as any direct financial interest related to a product addressed in the section of the guideline to which a Panel member contributes content. Financial interests include direct receipt by the Panel member of payments, gratuities, consultancies, honoraria, employment, grants, support for travel or accommodation, or gifts from an entity having a commercial interest in that product. Financial interests also include direct compensation for membership on an advisory board, data safety monitoring board, or speakers' bureau. Compensation and support provided to a Panel member's university or institution (e.g., grants, research funding) is not considered a conflict of interest. The co-editors strive to ensure that 50% or more of the members of each working group have no conflicts of interest.
Users of the guidelines	HIV treatment providers
Developer	Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV—a working group of the Office of AIDS Research Advisory Council (OARAC).
Funding source	The Office of AIDS Research (OAR), NIH
Evidence collection	The recommendations in the guidelines are based on studies published in peer-reviewed journals. On some occasions, particularly when new information may affect patient safety, unpublished data presented at major conferences or information prepared by the U.S. Food and Drug Administration or manufacturers (e.g., warnings to the public) may be used as evidence to revise the guidelines. Panel members of each working group are responsible for identifying relevant literature, conducting a systematic comprehensive review of that literature, and proposing updates to the guidelines based on the literature review.
Method of synthesizing data and formulating recommendations	Each section of the guidelines is assigned to a working group of Panel members with expertise in the area of interest. The members of the working group synthesize the available data. Recommendations are reviewed and updated by each working group after an assessment of the quality and impact of the existing and any new data. Aspects of evidence that are considered include but are not necessarily limited to the type of study (e.g., case series, prospective cohort, randomized controlled trial), the quality and appropriateness of the methods, and the number of participants and effect sizes observed. Finally, all proposed recommendations and supporting evidence are reviewed by the co-editors, OAR, subject matter experts at CDC and HIVMA/IDSA before final approval and publication.
Recommendation rating	Recommendations are rated according to the information in the table below, "Rating System for Prevention and Treatment Recommendations," and accompanied, as needed, by explanatory text that reviews the evidence and the working group's assessment. All proposed changes are discussed during teleconferences and by email and then assessed by the Panel's co-editors and reviewed by OAR, CDC, and IDSA before being endorsed as official recommendations.
Other guidelines	These guidelines focus on prevention and treatment of HIV-related OIs for adults and adolescents. A separate guideline outlines similar recommendations for children who have HIV infection. These guidelines are available on the <i>AIDSinfo</i> website (https://aidsinfo.nih.gov).

Guidelines Development Process, continued	
Topic	Comment
Update plan	Each working group leader and the co-editors meet every 3 months by teleconference to review interim data that may warrant modification of the guidelines. Updates may be prompted by approvals of new drugs, vaccines, medical devices or diagnostics, by new information regarding indications or dosing, by new safety or efficacy data, or by other information that may affect prevention and treatment of HIV-related OIs. In the event of new data of clinical importance, the Panel may post an interim announcement on the AIDSinfo website (https://aidsinfo.nih.gov) pending update of the guidelines with the appropriate changes.
Public comments	A 2-week public comment period follows release of a guidelines update on the AIDSinfo website. Comments received are reviewed by the appropriate work group(s) and the co-editors determine whether revisions to the guidelines are indicated. The public may also submit comments to the Panel at any time at contactus@aidsinfo.nih.gov .

How to Use the Information in these Guidelines

Recommendations in this report address:

1. Preventing exposure to opportunistic pathogens;
2. Preventing disease;
3. Discontinuing primary prophylaxis after immune reconstitution;
4. Treating disease;
5. When to start ART in the setting of an acute OI;
6. Monitoring for adverse effects (including immune reconstitution inflammatory syndrome [IRIS]);
7. Managing treatment failure;
8. Preventing disease recurrence (secondary prophylaxis or chronic maintenance therapy);
9. Discontinuing secondary prophylaxis or chronic maintenance therapy after immune reconstitution; and
10. Special considerations during pregnancy.

Recommendations are rated according to the criteria in the table, below, and accompanied, as needed, by explanatory text that reviews the evidence and the working group's assessment. In this system, the letters A, B, or C signify the strength of the recommendation for or against a preventive or therapeutic measure, and the Roman numerals I, II, or III indicate the quality of the evidence supporting the recommendation. In cases where there are no data for the prevention or treatment of an OI based on studies conducted in persons with HIV, but there are data derived from studies in persons without HIV that could plausibly guide management of patients with HIV, the recommendation is rated II or III but is assigned A, B, or C depending on the strength of the recommendation.

Rating System for Prevention and Treatment Recommendations	
Strength of Recommendation	Quality of Evidence for the Recommendation
A: Strong recommendation for the statement	I: One or more randomized trials with clinical outcomes and/or validated laboratory endpoints
B: Moderate recommendation for the statement	II: One or more well-designed, non-randomized trials or observational cohort studies with long-term clinical outcomes
C: Optional recommendation for the statement	III: Expert opinion

This document also includes tables in each section pertinent to the prevention and treatment of the OI(s) in that section, as well as eight summary tables at the end of the document ([Tables 1–8](#)), a figure of the *Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV*

latest Advisory Committee of Immunization Practices immunization recommendations adapted to adults and adolescents with HIV, and an appendix that summarizes recommendations pertinent to preventing exposure to opportunistic pathogens, including preventing exposure to sexually transmitted diseases (STDs) ([Appendix A](#)).

References

1. Bacchetti P, Moss AR. Incubation period of AIDS in San Francisco. *Nature*. 1989;338(6212):251-253. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/2922052>.
2. Alcabas P, Munoz A, Vlahov D, Friedland GH. Incubation period of human immunodeficiency virus. *Epidemiol Rev*. 1993;15(2):303-318. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/8174659>.
3. Bacchetti P, Osmond D, Chaisson RE, et al. Survival patterns of the first 500 patients with AIDS in San Francisco. *J Infect Dis*. 1988;157(5):1044-1047. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/3258900>.
4. Kaplan JE, Masur H, Holmes KK, et al. USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus: introduction. USPHS/IDSA Prevention of Opportunistic Infections Working Group. *Clin Infect Dis*. 1995;21 Suppl 1:S1-11. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/8547495>.
5. Palella FJ, Jr., Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. *N Engl J Med*. 1998;338(13):853-860. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/9516219>.
6. Detels R, Munoz A, McFarlane G, et al. Effectiveness of potent antiretroviral therapy on time to AIDS and death in men with known HIV infection duration. Multicenter AIDS Cohort Study Investigators. *JAMA*. 1998;280(17):1497-1503. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/9809730>.
7. Mocroft A, Vella S, Benfield TL, et al. Changing patterns of mortality across Europe in patients infected with HIV-1. EuroSIDA Study Group. *Lancet*. 1998;352(9142):1725-1730. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/9848347>.
8. McNaghten AD, Hanson DL, Jones JL, Dworkin MS, Ward JW. Effects of antiretroviral therapy and opportunistic illness primary chemoprophylaxis on survival after AIDS diagnosis. Adult/Adolescent Spectrum of Disease Group. *AIDS*. 1999;13(13):1687-1695. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10509570>.
9. Miller V, Mocroft A, Reiss P, et al. Relations among CD4 lymphocyte count nadir, antiretroviral therapy, and HIV-1 disease progression: results from the EuroSIDA study. *Ann Intern Med*. 1999;130(7):570-577. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10189326>.
10. Mocroft A, Ledergerber B, Katlama C, et al. Decline in the AIDS and death rates in the EuroSIDA study: an observational study. *Lancet*. 2003;362(9377):22-29. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/12853195>.
11. Buchacz K, Lau B, Jing Y, et al. Incidence of AIDS-Defining Opportunistic Infections in a Multicohort Analysis of HIV-infected Persons in the United States and Canada, 2000-2010. *J Infect Dis*. 2016;214(6):862-872. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/27559122>.
12. Mocroft A, Brettle R, Kirk O, et al. Changes in the cause of death among HIV positive subjects across Europe: results from the EuroSIDA study. *AIDS*. 2002;16(12):1663-1671. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/12172088>.
13. Gardner EM, McLees MP, Steiner JF, Del Rio C, Burman WJ. The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. *Clin Infect Dis*. 2011;52(6):793-800. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/21367734>.
14. Zandoni BC, Mayer KH. The adolescent and young adult HIV cascade of care in the United States: exaggerated health disparities. *AIDS Patient Care STDS*. 2014;28(3):128-135. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/24601734>.
15. HIV.gov. What is the HIV Care Continuum? 2016; <https://www.hiv.gov/federal-response/policies-issues/hiv-aids-care-continuum>. Accessed 3/22/2018.

16. Perbost I, Malafronte B, Pradier C, et al. In the era of highly active antiretroviral therapy, why are HIV-infected patients still admitted to hospital for an inaugural opportunistic infection? *HIV Med.* 2005;6(4):232-239. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16011527>.
17. Greenberg AE, Hader SL, Masur H, Young AT, Skillicorn J, Dieffenbach CW. Fighting HIV/AIDS in Washington, D.C. *Health Aff (Millwood)*. 2009;28(6):1677-1687. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/19887408>.
18. Berry SA, Fleishman JA, Moore RD, Gebo KA, Network HIVR. Trends in reasons for hospitalization in a multisite United States cohort of persons living with HIV, 2001-2008. *J Acquir Immune Defic Syndr.* 2012;59(4):368-375. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22240460>.
19. Centers for Disease Control and Prevention. Table 8 in Estimated HIV incidence and prevalence in the United States, 2010–2015. *HIV Surveillance Supplemental Report.* 2018;23(1). Available at: <https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-supplemental-report-vol-23-1.pdf>.
20. Dailey AF, Hoots BE, Hall HI, et al. Vital Signs: Human Immunodeficiency Virus Testing and Diagnosis Delays - United States. *MMWR Morb Mortal Wkly Rep.* 2017;66(47):1300-1306. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/29190267>.
21. Centers for Disease Control and Prevention. Monitoring Selected National HIV Prevention and Care Objectives by Using HIV Surveillance Data—United States and 6 Dependent Areas, 2015. *HIV Surveillance Supplemental Report.* 2017;22(2). Available at: <https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-supplemental-report-vol-22-2.pdf>.
22. HIV Continuum of Care, U.S., 2014, Overall and by Age, Race/Ethnicity, Transmission Route and Sex [press release]. July 27, 2017.
23. Panel on Antiretroviral Guidelines for Adults and Adolescents. Limitations to Treatment Safety and Efficacy. In: Department of Health and Human Services, ed. *Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV.* 2017.
24. Kelly C, Gaskell KM, Richardson M, Klein N, Garner P, MacPherson P. Discordant Immune Response with Antiretroviral Therapy in HIV-1: A Systematic Review of Clinical Outcomes. *PLoS One.* 2016;11(6):e0156099. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/27284683>.
25. Sonnenberg P, Glynn JR, Fielding K, Murray J, Godfrey-Faussett P, Shearer S. How soon after infection with HIV does the risk of tuberculosis start to increase? A retrospective cohort study in South African gold miners. *J Infect Dis.* 2005;191(2):150-158. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/15609223>.
26. Wood R, Maartens G, Lombard CJ. Risk factors for developing tuberculosis in HIV-1-infected adults from communities with a low or very high incidence of tuberculosis. *J Acquir Immune Defic Syndr.* 2000;23(1):75-80. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10708059>.
27. Wallace JM, Hansen NI, Lavange L, et al. Respiratory disease trends in the Pulmonary Complications of HIV Infection Study cohort. Pulmonary Complications of HIV Infection Study Group. *Am J Respir Crit Care Med.* 1997;155(1):72-80. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/9001292>.
28. Hirschtick RE, Glassroth J, Jordan MC, et al. Bacterial pneumonia in persons infected with the human immunodeficiency virus. Pulmonary Complications of HIV Infection Study Group. *N Engl J Med.* 1995;333(13):845-851. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/7651475>.
29. Engels EA, Rosenberg PS, Biggar RJ. Zoster incidence in human immunodeficiency virus-infected hemophiliacs and homosexual men, 1984-1997. District of Columbia Gay Cohort Study. Multicenter Hemophilia Cohort Study. *J Infect Dis.* 1999;180(6):1784-1789. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10558932>.
30. Gebo KA, Kalyani R, Moore RD, Polydefkis MJ. The incidence of, risk factors for, and sequelae of herpes zoster among HIV patients in the highly active antiretroviral therapy era. *J Acquir Immune Defic Syndr.* 2005;40(2):169-174. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16186734>.
31. Vanhems P, Voisin L, Gayet-Ageron A, et al. The incidence of herpes zoster is less likely than other opportunistic infections to be reduced by highly active antiretroviral therapy. *J Acquir Immune Defic Syndr.* 2005;38(1):111-113. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/15608535>.

32. Lawn SD, Butera ST, Folks TM. Contribution of immune activation to the pathogenesis and transmission of human immunodeficiency virus type 1 infection. *Clin Microbiol Rev*. 2001;14(4):753-777. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/11585784>.
33. Toossi Z, Mayanja-Kizza H, Hirsch CS, et al. Impact of tuberculosis (TB) on HIV-1 activity in dually infected patients. *Clin Exp Immunol*. 2001;123(2):233-238. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/11207653>.
34. Sadiq ST, McSorley J, Copas AJ, et al. The effects of early syphilis on CD4 counts and HIV-1 RNA viral loads in blood and semen. *Sex Transm Infect*. 2005;81(5):380-385. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16199736>.
35. Bentwich Z. Concurrent infections that rise the HIV viral load. *J HIV Ther*. 2003;8(3):72-75. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/12951545>.
36. Kublin JG, Patnaik P, Jere CS, et al. Effect of Plasmodium falciparum malaria on concentration of HIV-1-RNA in the blood of adults in rural Malawi: a prospective cohort study. *Lancet*. 2005;365(9455):233-240. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/15652606>.
37. Abu-Raddad LJ, Patnaik P, Kublin JG. Dual infection with HIV and malaria fuels the spread of both diseases in sub-Saharan Africa. *Science*. 2006;314(5805):1603-1606. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17158329>.
38. Centers for Disease Control and Prevention. Guidelines for prophylaxis against Pneumocystis carinii pneumonia for persons infected with human immunodeficiency virus. *MMWR Morb Mortal Wkly Rep*. 1989;38(Suppl 5):1-9. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/2524643>.
39. Masur H. Recommendations on prophylaxis and therapy for disseminated Mycobacterium avium complex disease in patients infected with the human immunodeficiency virus. Public Health Service Task Force on Prophylaxis and Therapy for Mycobacterium avium Complex. *N Engl J Med*. 1993;329(12):898-904. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/8395019>.
40. USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus: a summary. *MMWR Recomm Rep*. 1995;44(RR-8):1-34. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/7565547>.
41. USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus: disease-specific recommendations. USPHS/IDSA Prevention of Opportunistic Infections Working Group. *Clin Infect Dis*. 1995;21 Suppl 1:S32-43. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/8547510>.
42. Kaplan JE, Masur H, Holmes KK, et al. USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus: an overview. USPHS/IDSA Prevention of Opportunistic Infections Working Group. *Clin Infect Dis*. 1995;21 Suppl 1:S12-31. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/8547500>.
43. 1997 USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus. USPHS/IDSA Prevention of Opportunistic Infections Working Group. *MMWR Recomm Rep*. 1997;46(RR-12):1-46. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/9214702>.
44. 1999 USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus. U.S. Public Health Service (USPHS) and Infectious Diseases Society of America (IDSA). *MMWR Recomm Rep*. 1999;48(RR-10):1-59, 61-56. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10499670>.
45. Kaplan JE, Masur H, Holmes KK, Usphs, Infectious Disease Society of A. Guidelines for preventing opportunistic infections among HIV-infected persons--2002. Recommendations of the U.S. Public Health Service and the Infectious Diseases Society of America. *MMWR Recomm Rep*. 2002;51(RR-8):1-52. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/12081007>.
46. 1997 USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus: disease-specific recommendations. USPHS/IDSA Prevention of Opportunistic Infections Working Group. US Public Health Services/Infectious Diseases Society of America. *Clin Infect Dis*. 1997;25 Suppl 3:S313-335. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/9356832>.
47. 1999 USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus. *Clin Infect Dis*. 2000;30 Suppl 1:S29-65. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10770913>.

48. USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus: a summary. *Ann Intern Med.* 1996;124(3):349-368. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/8554235>.
49. 1997 USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus. *Ann Intern Med.* 1997;127(10):922-946. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/9382373>.
50. 1997 USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with HIV: Part I. Prevention of exposure. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention. *Am Fam Physician.* 1997;56(3):823-834. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/9301575>.
51. 1999 USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with HIV: part I. Prevention of exposure. *Am Fam Physician.* 2000;61(1):163-174. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10643957>.
52. Antiretroviral therapy and medical management of pediatric HIV infection and 1997 USPHS/IDSA report on the prevention of opportunistic infections in persons infected with human immunodeficiency virus. *Pediatrics.* 1998;102(4 Pt 2):999-1085. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/9826994>.
53. Kaplan JE, Masur H, Jaffe HW, Holmes KK. Preventing opportunistic infections in persons infected with HIV: 1997 guidelines. *JAMA.* 1997;278(4):337-338. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/9228443>.
54. Cruickshank DP, Wigton TR, Hays PM. Maternal physiology in pregnancy. In: Gabbe SG, Neibyl JR, Simpson JL, eds. *Obstetrics: Normal and Problem Pregnancies.* New York, NY: Churchill Livingstone; 1996.
55. Practice ACoO. ACOG Committee Opinion. Number 299, September 2004 (replaces No. 158, September 1995). Guidelines for diagnostic imaging during pregnancy. *Obstet Gynecol.* 2004;104(3):647-651. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/15339791>.
56. Toppenberg KS, Hill DA, Miller DP. Safety of radiographic imaging during pregnancy. *Am Fam Physician.* 1999;59(7):1813-1818, 1820. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10208701>.
57. Adelstein SJ. Administered radionuclides in pregnancy. *Teratology.* 1999;59(4):236-239. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10331526>.